

While not agreeing with the Examiner in this regard, this Continuation Application is being submitted with revisions to the claims corresponding to those proposed to be made in the parent application, so that the Examiner can properly consider the same.

In addition, the Examiner indicated in the Advisory Action that the IDS was not considered. The IDS is being re-submitted with this Continuation Application so that the contents may be considered by the Examiner. This new PTO-1449 also includes a listing of the references referred to in the disclosure. Copies of some of the references were provided in the parent filing. The missing copies will follow shortly.

In the Final Action in the parent application, the Examiner rejected claims 1 to 11 under 35 USC 112, second paragraph, as being indefinite, in view of the use of "consisting essentially of" in claim 1. The Examiner's suggestion to employ "consisting of" in claim 1 has been adopted. The same language is used in claim 27. It is submitted that claims 1 to 11 are no longer open to rejection under 35 USC 112, first paragraph.

In the Final Action on the parent application, the Examiner rejected claims 1 to 11 and 27 to 28 under 35 USC 102(a) as being anticipated by Baier et al.

The applicants' claims are directed to a recombinant conjugate antibody molecule which consists of a monoclonal antibody moiety specific for a surface structure of antigen presenting cells genetically modified to contain at least one antigen moiety exclusively at at least one preselected site on the monoclonal antibody, whereby the conjugate antibody molecule is capable of delivering the antigen moiety to the antigen presenting cells of a host and capable of eliciting an immune response to the antigen moiety. Applicants claims include immunogenic compositions comprising such molecule.

As previously pointed out, Baier et al teach the provision of a gp-120 peptide and antibody Fab fragments

89007093-011498

reactive with surface structures displayed on APCs. Such fusions are generated by DNA methodology. It is clear that the reference describes only the use of antibody Fab fragments in the chimeric molecules. The Examiner asserted in the Final Action on the parent application that applicants terminology "monoclonal antibody moiety" includes the Fab fragments of Baier.

It has previously been pointed out to the Examiner in the parent case that applicants employed a complete monoclonal antibody moiety. The Examiner asserts, however, that such limitation is not found in the claims. While not necessarily agreeing with the Examiner, the monoclonal antibody moiety now is defined in claims 1 and 2 as "bivalent". That the monoclonal antibody is bivalent is evident from consideration of applicants subsidiary claims. In this regard, it is noted that claim 3, for example, refers to "the heavy and light chains of said monoclonal antibody moiety". Accordingly, the monoclonal antibody moiety of claim 1 (said monoclonal antibody moiety) must contain both heavy and light chains and hence is bivalent. For further emphasis and to provide antecedent basis for the language of claim 3, claim 1 has been additionally amended to refer to the monoclonal antibody moiety possessing heavy and light chains.

It is submitted that the "monoclonal antibody moiety" recited in claim 1 is not anticipated by the Fab fragments disclosed by Baier et al. Even if the term were interpreted in the manner of the Final Action in the parent application, and thereby claim 1 arguably anticipated, it is abundantly clear that claims 3 to 11 cannot be considered anticipated since those claims specifically require that the monoclonal antibody moiety have both heavy and light chains, which clearly is not the case for the monovalent Fab fragment described by Baier et al.

Having regard to the revisions made to claim 1 and the above discussion, it is submitted that each of claims 1 to

09007093-011498

11 and 27 to 28 is not anticipated by Baier et al and hence claims 1 to 11, 27 and 28 are not open to rejection under 35 USC 102(a) as being anticipated by Baier et al.

In the Final Action on the parent application, the Examiner rejected claims 1 to 11, 27 and 28 under 35 USC 102(b) as being anticipated by or, in the alternative, under 35 USC 103(a) as being obvious over Barber et al U.S. Patent 4,950,480.

As previously noted in the prosecution of the parent application, the Barber et al reference is acknowledged in the specification, for example, on page 2, line 36 to page 3, line 10. As described therein, biotin-streptavidin based interaction was used to link antibody and antigen to provide a molecule used for targeting the antigen to the antigen-presenting cells. There are inherent disadvantages to the chemical coupling technique employed by Barber et al, such as yield (typically about 20%) and the variability between different preparations. There is no adequate control on the amount of coupled peptide, as well as the exact location of the reaction. Purification is usually required and losses of material can be significant. These disadvantages of the Barber et al system are echoed in the Baier reference in the paragraph bridging pages 2357 and 2358.

The present invention meets the need to produce conjugates of targeting antibodies and antigens of specific reproducible structure in high yields. In the present invention, as defined in claim 1, there is provided a recombinant conjugate antibody molecule which consists of a bivalent monoclonal antibody moiety having heavy and light chains and specific for a surface structure of antigen presenting cells, genetically modified to contain at least one antigen moiety exclusively at at least one preselected site on the monoclonal antibody moiety. This language defines a structure different from that provided by Barber et al.

09007093-011498

In the Final Action on the parent application, the

Examiner states:

"Examiner agrees that the process by which the antibody-antigen fusion proteins were generated are different. However, product by process is not patentably distinct in a product claim. Applicant is claiming antibody-antigen fusion proteins. The process by which the fusion proteins were generated is irrelevant. In order to demonstrate patentability, applicant must show that the recombinant antigen-antibody fusion proteins have properties which differ from the chemically conjugated fusion proteins." (Emphasis added).

Applicant agrees largely with this analysis. However, applicants claims recite structural limitations which distinguish the claimed product from those described in Barber, et al. Applicants claims recite that the monoclonal antibody moiety has been genetically modified to contain the antigen moiety exclusively at at least one preselected site on the monoclonal antibody moiety. This structural limitation is achievable only by recombinant methodology and hence the recitation of a recombinant conjugate antibody molecule also imparts a structural limitation on the molecule which differentiates the structure from that obtained in Barber et al.

The lack of adequate control on the amount of coupled antigen as well as the exact location of the reaction in the prior art of Barber et al ensures that the antigen moiety is not coupled exclusively at at least one preselected site into the monoclonal antibody moiety as required by applicants claims.

The Examiner further stated in the Final Action on the parent file that:

"... applicant argues the disadvantages in the chemical coupling technique. However, as applicant is claiming product claims, the advantages or disadvantages of the different methods used to obtain the product are irrelevant."

09007093-011498

However, as explained above, it is these very disadvantages of the method used which leads to the different structural features of claim 1 which differentiate from the cited prior art. By effecting the recombinant production claimed therein, it is possible to locate the antigen moiety exclusively at a preselected site on the antibody moiety, a result which is not obtainable using the biotin-streptavidin based interaction to link the antibody and antigen as in the case of the Barber et al U.S. Patent No. 4,950,480 reference.

Accordingly, it is submitted that claims 1 to 11 and 27 to 28 are not open to rejection under 35 USC 102(b) as anticipated by, or in the alternative, under 35 USC 103(a) as obvious over U.S. Patent No. 4,950,480.

In the parent application, the Examiner rejected claims 1 to 11, 27 and 28 under 35 USC 103(a) as being unpatentable over U.S. Patent No. 4,950,480 in view of U.S. Patent No. 5,196,520.

The Examiner, accordingly, made a third rejection of claims 1 to 11, 27 and 28 based on U.S. Patent No. 4,950,480:

- (A) anticipated by 4,950,480
- (B) obvious over 4,950,480 alone
- (C) obvious over 4,950,480 in combination with 5,196,320.

The necessity to make three rejections of the same claims shows a clear lack of conviction on the part of the Examiner as to the relationship of the claims to the prior art.

The Examiner stated in the Final Action on the parent application that the '320 patent:

"teaches the generation of single chain antibody fusion proteins. As the chains recite a monoclonal antibody moiety, the term would include single chain antibodies."

Applicants have discussed the Examiner's interpretation of the applicant's claim language above with respect to the rejection based on Baier et al. Applicant's claims now specifically recite that the monoclonal antibody has heavy and light

09007003-011498

chains, thereby clearly excluding the single chain antibody fusions such as are disclosed in the '320 patent.

Having regard to the applicant's claim language and having regard to the clear distinctions between applicants conjugate molecules and those disclosed in the '480 patent, it is submitted that the claims of this application are patentably distinguished from the combination of U.S. Patents Nos. 4,950,480 and 5,196,320 and hence claims 1 to 11 and 27 to 28 are not open to rejection under 35 USC 103 as unpatentable over the combination of prior art.

These amendments and arguments in support of patentability of the amended claims are submitted at this time in the interests of expediting prosecution.

It is proposed to amend the drawings and the description thereof in order to separately label the views contained within the Figures and in accordance with the description of the views of Figures 1 to 4 as contained on page 9, line 4 to page 10, line 3. In addition, the disclosure has been amended in order to indicate that Figures 6, 9 and 10 include multiple panels and to provide further identification of the panels. These changes correspond to those made in the parent filing.

It is believed that this application is now in condition for allowance and early and favourable consideration and allowance are respectfully solicited.

Respectfully submitted,

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